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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,657	11/28/2001	Sophie E. V. Martin	56297-5016-01	8313

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MORGAN LEWIS & BOCKIUS LLP  
1111 PENNSYLVANIA AVENUE, N.W.  
WASHINGTON, DC 20004

EXAMINER
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TUNG, JOYCE

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 03/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

*S-14*

**Advisory Action**

Application No.

09/994,657

Applicant(s)

MARTIN ET AL.

Examiner

Joyce Tung

Art Unit

1637

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 January 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: SEE THE ATTACHED.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-11.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

Following the entry of the amendment filed 1/26/2004, the claims 1-11 are pending.

1. Claims 1-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dower. (5,186,800).

Dower disclosed the method of the present invention is used to collect intracellular substances released from cells (See column 5, lines 21-25). The method is effective with wide variety of prokaryotic cells including both gram-positive and gram-negative bacterial cells (See column 4, lines 9-57). Dower discussed how the electrical conductivity of the medium or solution and the cell density are affecting on the electrical field (See column 4, lines 58-68 to column 5, lines 1-20). Conveniently, a non-conductive medium, such as water or sucrose is used for suspending the cells (See column 5, lines 19-20). Dower also disclosed that interelectrode spacing is critical in that it determines the electric field strength to which sample is exposed. (See column 6, lines 50-59). Usually, the electrode space is below 2.5 mm, preferably being in the range from 1.0mm to 2.0 mm (See column 6, lines 47-50). Dower further discussed the reasons to choose a precise electric field strength based upon the cellular dimensions, for example, smaller size bacterial, the voltage 10-15kV/cm is applied and larger size bacterial, the voltage 5 to 10 kV/cm is applied (See column 7, lines 44-52). Moreover, Dower discussed the duration applied cross the electrodes to promote the permeability of the cell wall. The precise voltage and pulse duration selected is depend on the nature of prokaryotic cell being treated. The pulse duration is generally be in the range from 2-20 sec or longer being in range from 3 to 10 sec (See column 8, lines 10-37). Finally, Dower indicates that the type of pulse waveform provided by the pulse generator is not critical (See column 7, lines 53-57).

Dower does not disclose applying the voltage not more than 50 volts including the range of the voltage between 0.5-50 volts, and the period for applying voltage is at least 30 seconds or 2 minutes continuously.

However, based upon the discussion of the factors which affects the permeability of the bacterial cells in the teachings of Dower it would have been prima facie obvious for one of ordinary skill in the art at the time of the instant invention to apply the electroporation of Dower to release intracellular material from bacterial cells with the optimization of the amount of volts, and the time needed for the pulse. The motivation to vary the voltage is to avoid the denaturation of intracellular material. The electric conductivity of the medium or suspension and the duration of the electrical field as discussed by Dower would have been taken into consideration by one of ordinary skilled in the art at the time of the instant invention to release intracellular material from cells by applying a continuous voltage of not more than 50 volts to a suspension. Thus it would have been prima facie obvious to apply a continuous voltage not more than 50 volts to release intracellular material from cells in a cellular suspension.

The response argues that Dower taught the duration of voltage pulse which is 2 to 20 msec. The newly amended language exclude millisecond pulses. Nevertheless, Dower also taught that the electrical pulse will generally be preferable within 30 seconds with many prokaryotic cells to remain permeable for some time after exposure to the electrical pulse (See column 8, lines 39-48). Although, Dower does not suggest applying the voltage which is not more than 50 volts to a suspension containing cells, it would have been prima facies obvious for one of ordinary skill in the art at the time of the instant invention to apply the electroporation of Dower to release intracellular material from bacterial cells with the optimized amount voltage and the time for the pulse as discussed in the paragraph above. Therefore, the rejection is maintained.

2. The rejection of claims 1-11 under 35 U.S.C. 112, second paragraph is withdrawn.

*Summary*

3. No claims are allowable.
4. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung *JT*  
February 25, 2004

*Jeffrey Siew*  
JEFFREY SIEW  
PRIMARY EXAMINER  
*2/26/04*